

# CPD — Education and self-assessment

## Surgery for epilepsy

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While medical treatment remains the first line of treatment for epilepsy, surgery provides effective long-term control in suitable patients. Detailed investigations are necessary to prove suitability and in order to choose the appropriate procedure. This article gives an outline of the investigative programme and the various operative approaches. Novel methods and those under investigation are also discussed.

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### INTRODUCTION

Epilepsy has been experienced by humanity throughout history. Ever since the first recorded description in Akkadian, the oldest written language, for thousands of years supernatural causes were thought to be behind the observations. A long list of great minds grappled with the condition but without knowledge of electricity or the structure and function of neurons, etc., all such efforts were futile. The last two centuries of scientific and medical achievements resulted not only in a more realistic understanding of the epileptic phenomena but also in the development of numerous pharmacological interventions.

Surgical treatment, although usually considered a new development in management, also goes back to trephinations of ancient times as no doubt many of those thought to suffer from 'evil spirits' must have presented with seizures. Epilepsy surgery in its modern sense belongs to the 19th and 20th centuries, as it was necessary for Broca and others to recognize localization of cerebral functions in the second half of the 19th century before these interventions would have any chance of success. The first heroic brain

operations of the modern era were performed for abscesses and tumours. Victor Horsley's published series of epilepsy surgery cases in 1887 were the catalysts, which led to the magnificent development of neurosurgery in general, and epilepsy surgery in particular. Foerster, Krause, Penfield and other great early pioneers stimulated further systematic and strictly science-based work of Talairach and Szikla in Paris, Faulkner in London and Yaşargil in Zurich. It will not be strange to the reader that the long list still continues today.

Surgical treatment ought to be considered for all medically intractable seizures. Medical failure is the fate of approximately 30% of people with newly diagnosed epilepsy and the incidence is approximately 6 per 100 000 per year. The reader of this review will be well familiar with the social, economic, psychological and other disastrous effects of intractable epilepsy. Intractability is associated with an increased mortality. Sudden unexpected death in epilepsy (SUDEP) is more common in patients with more severe epilepsy e.g. those entered into drug trials or investigated with view to surgery.

## WHO SHOULD BE CONSIDERED?

An Epilepsy Surgery Programme starts with the process of identifying medically refractory patients with epilepsy. In the past, intractability was defined very loosely and thus the patient cohorts were different in various series. There were different requirements between centres for seizure frequency, length of drug treatment and the number of drugs tried. Most experts define intractable epilepsy when the patient has true epileptic seizures of unacceptable frequency and severity after a trial of at least two drugs up to tolerance level for a period of 2 years. A careful balance must be found to avoid missing the chance of medical control by rashly offering surgery on one hand and undue prevarication on the other. Having said that, there is some evidence that the sooner surgery is performed the better the eventual post-surgical seizure control. Long-term integration into society and better psychosocial outcome can then be achieved.

## INVESTIGATIONS

In order to identify those patients with the best chance of successful surgical outcome, investigations are designed to answer the following questions:

- (1) Are the seizures truly epileptic?
- (2) Is there a focal onset?
- (3) Is it a single focus?
- (4) Is it in a site where it can be excised without neurological deficit?

Analysis and classification of seizures and the epileptic syndrome is very important. Detailed history includes previous events of infection in the nervous system, trauma, family history, etc. The range of previous drugs used and compliance is recorded. Inter-ictal or ictal focal neurological features serve as useful pointers. Neuropsychological assessment not only lateralizes dominance but the likely localization of speech and memory serves as a useful baseline for later follow-up. Assessment of expectations by the patient and his/her carer is crucial in order to help develop a coping strategy with the possibility of being turned down for surgery or indeed for the possibility of failure after the operation. General contra-indications to surgery (acute psychiatric disorder, neurodegenerative disorders, medical contra-indications, etc.) are established.

Radiological evaluation is classically performed by structural and functional imaging. The former is performed using Magnetic Resonance Imaging (MRI) scanning, supplemented by CT scanning or cerebral

angiography as appropriate. The first level of MR analysis may identify a diffuse or a focal abnormality. Examples of the former would be signs of previous infection or trauma or indeed a widespread mal-development of the cortical structures. Focal abnormalities may include vascular or neoplastic lesions. Already at this level mesial temporal sclerosis may be identified. The relevance of this first level analysis is that a positive result dramatically reduces the need for detailed, time- and resource-intensive investigations. The second level of lesion detection requires specific sequences, which highlight otherwise less obvious pathological foci, e.g. cavernomas or mesial temporal sclerosis. T2 relaxometry gives a quantitative measure of mesial temporal sclerosis, thereby enhancing the diagnosis obtained by visual inspection of images. Measurements of hippocampal volume further increase sensitivity. Three-dimensional reconstruction of cortical structures can demonstrate malformations of cortical development which are otherwise difficult to detect.

A novel way of using MRI is functional imaging. Execution of simple tasks (e.g. finger tapping) during scanning demonstrates the active cortex that would have to be preserved in the vicinity of a focal lesion. Positron emission tomography (PET) may be helpful showing focal inter-ictal reduction in metabolism and single photon emission tomography (SPECT), when performed ictally, shows focal increase in blood flow. These images can be co-registered with high resolution structural images to guide the surgeon with intra-operative use of neuronavigation (the inter-active demonstration of surgical instruments in relation to pre-operative structural images, a kind of 'global positioning system' in the brain).

Electrophysiological evaluation classically starts with inter-ictal scalp EEG. In many patients the findings on this simple level exclude the possibility of focal surgery by demonstrating clear multi-focal seizure onset. The temporal relationship between clinical and EEG findings is established by video telemetry while at the same time pseudo-seizures are excluded. Detailed discussion of EEG analysis is, of course, beyond the scope of this review. Suffice it to say that an increasingly invasive data acquisition is needed for cases where there is the slightest incongruence in the available data. This is provided by the use of sphenoidal and foramen ovale electrodes and with electrodes placed surgically into the extradural or subdural space or indeed direct into the parenchyma using stereotactic guidance techniques. Electro-corticography and cortical stimulation may be carried out during the definitive operation.

A further two investigations deserve a mention. Magneto-encephalography is a promising emerging technique that records the magnetic fields related

to inter-ictal epileptiform discharges. It is still an experimental technique, but, particularly when combined with MRI images, it may in the future contribute to the identification of the irritative zone (area of cortex generating inter-ictal spikes) although not the actual seizure onset zone. The other important pre-surgical test is the so-called WADA test. This test consists of 'anaesthetizing' one and then the other hemisphere whilst neurological and neuropsychological assessment is carried out. The main role is to evaluate whether memory function would be maintained by the contra-lateral hemisphere when the site of the epileptogenic zone is inactivated. The test also provides data for lateralization of the language function.

## SURGICAL TECHNIQUES

Surgical approaches can be classified in a didactic manner into:

- (a) removal or destruction of the focus;
- (b) isolation of the focus;
- (c) functional operations (neurostimulation).

Another suitable classification would line up the procedures by a decreasing level of invasiveness with hemispherectomy on one (most invasive) end and vagus nerve stimulation on the other (least invasive) end of the scale. However, it would appear most appropriate to describe first the commonest procedure, surgery for mesial temporal sclerosis.

### Surgery for mesial temporal sclerosis

About two-thirds of patients with localization related epilepsy suffer from mesial temporal sclerosis and present with complex partial seizures. The condition is characterized by a strong association of injury to the medial structures of the temporal lobe in early childhood, often a febrile seizure, and investigations demonstrate atrophy and signal change in the mesial structures of the temporal lobe. A closely related but aetiologically distinct entity is lesion related temporal lobe epilepsy in which there is a lack of history of early injury but imaging demonstrates a benign neoplasm (glioma, dissembrioplastic neuroepithelial tumour, ganglioglioma, etc.) of vascular malformation (arteriovenous malformation or cavernous venous malformation) in the same site. Developmental lesions of the area also fall into this category.

The standard operation is anterior medial temporal resection ('temporal lobectomy'). It is performed

through a question mark shaped incision and a standard temporal craniotomy. The vessels on the convexity surface of the temporal lobe are diathermized and divided in line with the marked posterior boundary and this is carried down along the undersurface of the temporal lobe. At a depth of about 3 cm the incision is turned anteriorly and thus the lateral neo-cortex is disconnected and removed. Using the ultrasonic aspirator the removal proceeds medially to enter the lateral ventricle. The ventricular part of the hippocampus is displayed and the posterior end is marked. The choroid plexus and the optic tract are carefully protected from injury. The amygdala and the head of the hippocampus are dissected from the arachnoid medially, the hippocampus is divided at the tail and usually a 4 cm long specimen is removed en masse.

As the target of resection in most of these cases is the medial set of structures rather than the cortex, Niemeyer described a less invasive approach. In this procedure the lateral ventricle is entered through a transcortical incision and through this access is gained to the amygdala and about a 3 cm long section of the hippocampus, and these structures are removed.

In order to further reduce the impact on the cortex, Yaşargil devised a method to reach the mesial temporal structures entering the ventricle after opening the Sylvian fissure and retracting the temporal operculum. This procedure, although technically more demanding, allows the preservation of neocortical structures in the lateral temporal lobe. Selective amygdalohippocampectomy is performed through the standard pterional craniotomy, used for the majority of operations performed for clipping of aneurysms and removal of skull base tumours. The Sylvian fissure is opened using mainly sharp dissection combined with the spreading action of fine forceps. This procedure is carried out with extreme care and patience in order to avoid any injury to the middle cerebral artery branches and when the internal carotid artery and its branches are exposed, particular care is taken to identify and protect the anterior choroidal artery. This artery is a very useful marker in guiding the surgeon to the plane of the choroidal fissure and thus aids the entrance into the temporal horn. The ventricle is entered by making a small, about 15 mm, incision in the reflection between the temporal operculum and the insula. First the amygdala is found and removed with gentle suction leaving the most medial part intact. Entering the lateral ventricle gives a useful confirmation of orientation. The ventricle is opened wide to display the hippocampus. The uncus, the hippocampus and parahippocampus are removed preferably in one block after a circular dissection and mobilization carried out down to the subpial plane. After subpial resection of the medial basal area of the temporal pole the structures lying on the other

side of the pia/arachnoid (anterior choroidal artery, optic tract, ocular motor nerve, etc.) are inspected and meticulous haemostasis achieved. Surgical results depend on the quality of patient selection and the pathological findings. Increased severity of gliosis in the removed specimen is associated with better seizure control. Usually a 55–85% seizure free state can be achieved.

### Extratemporal resective surgery

Resections of extratemporal foci have generally been substantially less successful than temporal resections, particularly in the absence of visible structural lesions. This may be for several different reasons: the epileptogenic zone may be more diffuse, the seizures may have a rapid spread or there is no 'typical' anatomical structure (like the hippocampus in the temporal lobe) where the focus may usually lie. Perhaps even more important is the fact that the epileptogenic zone in extratemporal epilepsy often encroaches upon eloquent areas and this limits the extent of safe resection. Extratemporal resections are, therefore, almost invariably preceded by invasive recording (subdural grid placements and recording as well as cortical stimulation). The latter is particularly important in planning cortical resections. In most centres cortical stimulation is carried out using awake craniotomy in order to avoid causing post-operative neurological deficit. Intra-operative cortical stimulation revealed an extreme variability of essential language sites, even in areas considered safe on anatomical landmarks. It is possible, and it appears increasingly likely, that functional MRI scanning linked with intra-operative neuronavigation may allow omission of the rather cumbersome intra-operative electrocortigraphy in the future.

### Hemispherectomy/hemispherotomy

*Hemispherectomy* is the most radical and invasive operation carried out for epilepsy. Suitable candidates for this operation are usually children, who have widespread hemispheric damage. This may be caused by Rasmussen's encephalitis (a chronic encephalitis leading to progressive atrophy of one hemisphere), Sturge–Weber Syndrome, hemi-megaloencephaly or major single-hemispheric trauma. There is usually severe impairment in contra-lateral hand function with better proximal upper limb and often quite good lower limb function.

The first such operations, the entire removal of the hemisphere, resulted in severe and often fatal long-term complications. The surgical techniques subse-

quently underwent an evolution towards less and less invasive approaches. Functional hemispherectomy includes extensive temporal lobe and large posterior frontal/parietal resection leaving the frontal and occipito-parietal lobes disconnected but vascularized.

*Hemispherotomy* disconnects the whole epileptogenic hemisphere from the subcortical centres and from the other hemisphere. Different techniques have been described and appear to have less complications than hemispherectomy with comparably good seizure control for both of these operations (about 80% of patients becoming seizure free and another 15% improve). These operations are technically challenging though they may be made easier by an enlarged ventricle on the side of the hemispheric damage seen in the majority of these conditions.

### Corpus callosotomy

The procedures described in the previous part of this review were designed either to remove or entirely isolate the epileptogenic focus. However, there are many patients with poorly controlled epilepsy who have no identifiable, resectable, single focus and who are thus not suitable for the operations described earlier. The aim of callosotomy is to disrupt the propagation of spreading seizure discharges from one to the other hemisphere. This disconnection procedure was introduced first for patients who had uni-hemispheric seizure onset with secondary generalization to the other hemisphere but whose diseased hemisphere maintains useful neurological function. Later it has been found that patients with sudden drop attacks responded well to callosotomy. Useful improvement was also observed in patients with Lennox–Gastaut Syndrome, frontal lobe epilepsy and multi-focal epilepsy. The indications for this operation may be broadened to many more medically intractable disabling seizures, untreatable by other surgical methods. This would suggest that this operation should be performed on a very large number of patients. In reality, the acceptance of this operation was limited by the operation being highly invasive with relatively high complication rate. Seizure outcome can be approximately summarized as one-third becoming fit free, one-third not responding and the final third showing some degree of seizure reduction.

### Multiple subpial transections (MST)

This is another non-resective surgical technique. The indication for this operation is a well-identified epileptic focus residing in an indispensable cortical



area (motor cortex, speech area, etc.). The rationale behind the procedure is the vertical, columnar, arrangement of functional outflow from the cortex and the theory that propagation of epileptic activity from the focus is predominantly horizontal. The operation was first described by Morrell. First the epileptogenic area is identified using non-invasive techniques and invasive recording. After the area is carefully marked, multiple cuts are made in the cortex using a hook-shaped knife, at right angles to the long axis of the gyrus. Repeated similar cuts are then made parallel with the first one, every 5 mm or so. By this process small independent slice-shaped sections are isolated from each other whilst allowing their useful outflow vertically. The operation is very time consuming but gradually it finds its way into the epilepsy surgery practice of many centres.

### Gamma knife surgery (stereotactic radiosurgery)

Lars Leksell introduced the term 'radiosurgery' in 1951, to the application of high energy converging photon beams to a single point within the brain. It achieves its effects by either necrosis or by other, subtler, alteration of function in a small volume of the brain with relatively little effect on the rest. First it was applied in functional neurosurgery making deep brain lesions. Subsequently it was tried successfully in the management of a wide range of pathologies including tumours and arteriovenous malformations. After treating AVMs associated with focal onset epilepsy, many observed an improvement or cessation of epileptic activity. This prompted treatment of small indolent gliomas, cavernomas and other pathologies and good seizure control results were observed. Since 1995 Regis presented several patients with mesial temporal sclerosis being treated using focussed radiation with the gamma knife. Other centres, including the authors', followed suit treating a small series of patients. Our experience showed that seizure control at 3 years following irradiation is very similar to temporal lobe resections and thus this method can be advocated for those who are unable or unwilling to undergo resective surgery. However, our observation was that there is a long, 12–36 months, lag-time to achieve the seizure free state. Furthermore, some patients found it difficult to cope with the slow alteration of their seizure pattern and the appearance of very frequent auras for some months.

In our small series we have not observed permanent neurological deficit but about 50% of patients required several weeks of dexamethasone treatment due to focal cerebral swelling after about 1 year. The method certainly deserves to be exposed to wider scale trials but its role is not yet established.

### Vagus nerve stimulation

An entirely new class of operations for epilepsy utilizes neural stimulation. Over the past decades stimulation of the thalamus and cerebellum were found to have some antiepileptic properties and in selected centres series of patients were implanted with these devices. In spite of enthusiasm by some authors, those operations went out of fashion when exposure to randomized studies failed to show them to be effective.

However, based on solid experimental studies using various animal models of epilepsy, stimulation of the vagus nerve took over as the sole representative of neurostimulative operations in the current surgical armamentarium. The mechanism of action is far from clear although the pathway, via the nucleus of the solitary tract, has been demonstrated. As electronic technology reached the sophistication and miniaturization to make an implanted device practical, it was gradually introduced in many centres. The lack of intracranial surgical invasion and the relatively small surgical procedure allowed it to spread rapidly. Currently it is used predominantly for indications similar to corpus callosotomy and indeed it appears likely that this procedure will take over the role of that more invasive operation. Apart from being minimally invasive, the operation has the unique property of improving, rather than suppressing, mood and cognitive function. For a more detailed analysis of this new technique please refer to the previous article by Boon *et al.*

### FURTHER READING

1. Luders, H. O. and Comair, Y. G. (Eds) In: *Epilepsy Surgery*. 2<sup>nd</sup> Edition. Philadelphia, Lippincott Williams & Wilkins, 2001.
2. Wiebe, S., Blume, W. T., Girvin, J. P. *et al.* A randomised, controlled trial of surgery for temporal lobe epilepsy. *New England Journal of Medicine* **345**: 311–318.
3. Engel, J. Jr (Ed.) In: *Surgical Treatment of the Epilepsies*. 2<sup>nd</sup> Edition. New York, Raven Press, 1993.